Title: CARDIOPULMONARY BYPASS AND TOTAL CIRCULATORY ARREST ALTERS CEREBRAL METABOLISM IN INFANTS

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Introduction: Cardiopulmonary bypass (CBP) management in infants and children involves extensive alterations in temperature (18-37°C) and perfusion pressure, with occasional periods of circulatory arrest. Despite the use of these biological extremes of temperature and perfusion, their effects on cerebral metabolic rate (CMRO2) are unknown. This study was designed to examine the effect of hypothermic CPB in children with and without periods of total circulatory arrest on CMRO2 and to determine the temperature coefficient (Q10), which defines the relationship of temperature to CMRO2.

Methods: After Institutional Review Board approval and informed parental consent, CPB and CMRO2 were measured in 46 infants and children, ages 1 day - 9 years, undergoing repair of congenital heart defects. Patients were grouped based on CPB conditions: 1) moderate hypothermic CPB (MHCBP) at 28°C with continuous flow, 2) deep hypothermic CPB (DHCBP) at 18-20°C with continuous flow and 3) deep hypothermic CPB at 18-20°C with total circulatory arrest (DHCA). CPB was measured using xenon clearance methodology. Using a jugular venous bulb catheter, cerebral venous oxygen content was directly measured, and CMRO2 and oxygen extraction (CaO2 - CoO2) were determined. Measurements were made before CPB (stage A); during stable hypothermic CPB (stages B + C) or at stable hypothermic CPB immediately before and after DHCA (B + C); rewarmed on CPB (stage D); and after CPB (stage E). To examine the relationship of temperature to CMRO2, the temperature coefficient (Q10), defined as the ratio of metabolic rates at two temperatures separated by 10°C, was determined from data from the stages A (baseline at 36°C) and B (CPB, cold) for each group. Data was analyzed using paired t-tests and linear regression techniques.

Results: See Table. All 3 groups showed a significant decrease in CPB and CMRO2 during hypothermic bypass conditions at stage B compared to prebypass levels (A) (p < 0.001). In the MHCBP and DHCBP groups, CPB and CMRO2 remained reduced during rewarming after circulatory arrest at stage D and persisted after being weaned from bypass at stage E. The Q10 for the MHCBP, DHCBP and DHCA groups were 3.2, 4.1 and 5.1 respectively.

Discussion: These data demonstrate several new findings: 1) CPB and CMRO2 are significantly reduced during hypothermic CPB in children, principally related to temperature reduction. Q10 quantifies this relationship and shows a considerably greater Q10 for the deep hypothermic groups (DHCBP, DHCA). The striking increase in Q10 going to 18-20°C proves that the known protective effect of deep hypothermia for circulatory arrest up to periods exceeding 1 hour can be explained on a metabolic basis alone. 2) After rewarming from DHCA, CPB and CMRO2 remain reduced, suggesting post-ischemic hyperperfusion and a metabolic disturbance in oxygen utilization. In the presence of low flow after DHCA, these patients are unable to increase oxygen extraction to meet tissue demands during rewarming and after CPB.

<table>
<thead>
<tr>
<th>Group</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>MHCBP group</td>
<td>31.6±.2</td>
<td>18.4±.2</td>
<td>25.9±.2</td>
<td>31.1±.2</td>
<td>44.1±.7</td>
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<tr>
<td>DHCBP group</td>
<td>20.8±.3</td>
<td>18.0±.2</td>
<td>25.9±.2</td>
<td>31.1±.2</td>
<td>44.1±.7</td>
</tr>
<tr>
<td>DHCA group</td>
<td>19.6±.5</td>
<td>18.0±.2</td>
<td>25.9±.2</td>
<td>31.1±.2</td>
<td>44.1±.7</td>
</tr>
</tbody>
</table>

Note: values ±SD; CBF and CMRO2×1000 (μmol/kg/min); CaO2-CoO2 = oxygen extraction

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Title: THE PROPHYLACTIC EFFECT OF INTRAVENOUS ENALAPRILAT ON INTRAOPERATIVE HYPERTENSION

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Introduction: Although angiotension-converting enzyme inhibitors (ACEI) are effective in the therapy of essential hypertension, conflicting reports have appeared in the literature with regard to the benefit of ACEI for the treatment of intraoperative hypertension. Yates and Hunter (1) found that pretreatment with enalaprilat, an oral ACEI, reduced the pressor response associated with intubation. In contrast, Murphy et al. (2) did not reach this conclusion with intravenously-administered enalaprilat, the active metabolite of enalaprilat. We designed a double-blind, placebo-controlled study to evaluate the effect of intravenous enalaprilat on intraoperative cardiovascular stability.

Methods: After IRB approval and informed consent, 10 ASA I-II patients scheduled to undergo limb surgery, ages 18-75, were randomized to receive enalaprilat (1.25 mg) or placebo intravenously 20 minutes prior to intubation. Each patient was premedicated orally with 5 mg diazepam. Anesthesia was induced with thiopental (4 mg/kg with 50 mg increments as required) and fentanyl (2 μg/kg). Either vecuronium (0.1 mg/kg) or succinylcholine (1.5 mg/kg) was randomly used for muscle relaxation. Anesthesia was maintained with 60-70% N2O/O2 and fentanyl (50 μg increments up to 200 μg/hr). Ethane was administered to control elevations in blood pressure, if necessary. Blood pressure and heart rate were recorded every 2 minutes using an automated blood pressure cuff. Statistical analyses were performed by ANOVA with repeated measures using an LSD test for a comparison of means; p<0.05 was considered to be statistically significant.

Results: Blood pressure and heart rate data are presented in Figure 1 and Figure 2, respectively. There was a significant elevation in both the pressor response (p<0.005) and heart rate (p<0.005) following intubation in the placebo group. There were no hypotensive episodes during the intraoperative period in either the enalaprilat-treated or placebo group.

Discussion: The improved hemodynamic stability here, coupled with the absence of hypotensive incidence, supports the use of enalaprilat to control intraoperative hypertension. This may be especially beneficial in those patients with cardiovascular and cerebrovascular disease who are at risk from the complications related to hypertension and tachycardia.

References
1. Anesthesia 43: 935-938, 1988

Figure 1

Figure 2